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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/524,454	03/10/2000	Kristian Berg	697.013US1	5804

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SCHWEGMAN, LUNDBERG & WOESSNER, P.A.
P.O. BOX 2938
MINNEAPOLIS, MN 55402

EXAMINER	
EWOLDT, GERALD R	
ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
08/04/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

uspto@slwip.com
request@slwip.com

Office Action Summary	Application No.	Applicant(s)	
	09/524,454	BERG ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 May 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,4,8-10,28-32,37,41 and 42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,4,8-10,28-32,37,41 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment and remarks filed 5/28/10 are acknowledged.

2. Claims 2, 4, 8-10, 28-32 ,37 41, and newly added Claim 42 are pending and being acted being acted upon.

3. In view of Applicant's amendment the previous rejection of Claim 41 has been withdrawn.

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 2, 4, 8-10, 28-32 ,37 41, and newly added Claim 42 stand/are rejected under 35 U.S.C. 102(b) as being anticipated by WO 96/07432 (IDS).

As set forth previously, WO 96/07432 teaches a method of expressing [now presenting an antigenic molecule on the surface of a viable cancer cell], said method comprising:

contacting said cell *in vitro* [and *ex vivo*] with said antigenic molecule [now peptide] (including a vaccine component, a molecule capable of stimulating an immune response, and a peptide, also including an antigen bound to a carrier molecule) and with a photosensitizing agent (a porphyrin, phthalocyanine, purpurin, chlorin, benzoporphyrin, naphthalocyanine, cationic dye, and tetracycline, including $TPPS_4$, $TPPS_{2a}$, and $AlPcS_{2a}$, also including a photosensitizing agent bound to a carrier molecule), wherein said molecule and said agent are each taken up into an intracellular membrane-restricted compartment of said cell; and irradiating said cell with light of a wavelength effective to activate the photosensitizing agent, such that the membrane of said intracellular compartment is disrupted, releasing said molecule into the cytosol of the cell, without killing the cell by irradiation, wherein, said released antigenic molecule, or a part thereof of sufficient size to generate an immune response, is subsequently presented on the surface of said cell by a class I MHC molecule (see particularly the claims). Note that reference does not specifically state that the method results in the cell surface expression of the antigen in MHC Class I, however, the reference teaches the same steps as those of the instant claims, thus, said same steps would inherently result in the same outcome, i.e., the claimed method of the expressing an antigenic molecule on the surface of a viable cell. The reference further teaches the *in vivo* administration of and antigen and photosensitizing agent (page 6), thus, Claim 37 has been included in the rejection.

WO 96/07432 is clearly not limited to the internalization of toxic molecules, nor to gene therapy nor to *in vitro* internalization, i.e., the exemplified embodiments as Applicant argues. The three methods at pages 7-8 are disclosed only as "Examples of experimental and clinical utilization". Further, see for example Claim 2 wherein the internalized compounds include, "sugars, proteins, and peptides", none of which are required to be toxic and all of which can be antigens depending on the context. Indeed, at page 2 (as well as in the Abstract) of the reference it is taught that the method is performed, without destroying the functionality of the majority of the cells." After the release of the internalized compound into the cytosol of a live cell processing and presentation on MHC class I would be an inherent property.

Further, a review of the instant specification discloses at page 4:

"WO 96/07432, on the other hand, is concerned with methods which use the photodynamic effect as a mechanism for introducing otherwise membrane-impermeable molecules into the cytosol of a cell in a manner which does not result in widespread cell destruction or cell death. In this method, the molecule is co-internalised (more particularly , "endocytosed") into an intracellular vesicle in the cell (e.g. a lysosome or endosome) together with a photosensitizing agent. The cell is then exposed to photoactivating light which "activates" the photosensitizer, which in turn causes the vesicle membrane to disrupt or rupture, releasing the vesicle contents, including the molecule, into the cell interior i.e. the cytosol. It was found that in such a method the functionality or the viability of the majority of the cells was not deleteriously affected. Thus, the utility of such a method, termed ,"photochemical internalization" was proposed for transporting a variety of different molecules, including therapeutic agents, into the cytosol i.e. into the interior of a cell".

And at page 12 the specification discloses:

"The photochemical internalization process is described in more detail in WO 96/07432 (the contents of which are incorporated herein by reference). Methods of PDT are now widely described in the literature."

Clearly, at the time of the invention, Applicant's viewed the teachings of the WO document as broader than they now argue. The reference clearly teaches the introduction of molecules into cells without killing them. The reference also teaches the introduction of molecules into cancer cells. Thus, the reference anticipates the method of the instant claims. Accordingly, the reference teaches the method of the instant claims. Therefore, the outcome of said method must be the same, i.e., expression or presentation of the antigenic peptides on the cell surface is inherent.

Applicant's arguments, filed 5/28/10 have been fully considered but they are not persuasive. Applicant argues that the reference cannot anticipate the claimed method because it lacks "key details", i.e., because of "missing matter".

As set forth above, the reference teaches the claimed method steps performed on viable cancer cells thus, the same outcome must follow.

Applicant admits at page 8, paragraph 1, that WO 96/07432, "expressly teaches that the molecules are internalized within cells", but "not cell surface presentation of antigenic peptides".

Applicant has provided no convincing reasoning why said presentation would not follow in a viable cell.

Applicant argues that the disclosure of WO 96/07432 on cancer treatment is "very limited".

Applicant is reminded that the claimed method is not a method of treating cancer but merely a method of, "presenting an antigenic peptide on the surface of a viable cancer cell" (Claim 2).

Applicant argues that the "Examiner's allegations are contrary to binding case precedent" citing *In re Zurko*.

Applicant is advised that *Zurko* concerned the creation of a secure computer environment in the context of a rejection for obviousness. To call any decision in that case "binding case precedent" in the instant case is not a convincing argument.

In discussing WO 96/07432 and the issues therein "in more detail", Applicant further admits, "the WO 96/07432 method allows molecules to be introduced into the cytosol of viable cells by photochemical internalization without significant cell death, and the photointernalization procedure does not destroy cells as does the PDT procedure".

And cell surface presentation would then follow.

Applicant argues that the generic disclosure of WO 96/07432 cannot anticipate species claims.

The claims of the instant application appear themselves to be generic in nature.

Applicant continues the argument that WO 96/07432 does not teach killing cells or the treatment of cancer. Applicant selectively cites the document in support, e.g., page 7, lines 5-18, Examples 2 and 4, Figures 3 and 5, etc.

Again, the instant claims are drawn to a method of "presenting an antigenic peptide on the surface of a viable cancer cell" (Claim 2).

Applicant concludes:

> "The teachings by WO96/07432 in relation to cancer are therefore limited and concern only methods in which cell death is the final result of the photointernalization method. As Applicants' claims relate to cancer cells, the only relevant disclosure by WO96/07432 is its teachings on cancer treatment. To suggest that the document teaches the use of other molecules for internalization into cancer cells goes beyond the disclosure of the document in relation to cancer. Furthermore, the cells disclosed by W096/07432 are not in contact with cytotoxic T cells and thus the required feature of claim 2 cannot be achieved. Hence, Applicants submit that the teachings and examples provided in WO96/07432 fall outside the scope of Applicants' claims."

Note particularly Applicant's argument, "To suggest that the document teaches the use of other molecules for internalization into cancer cells goes beyond the disclosure of the document in relation to cancer". First, a review of the entire document, and particularly Claim 12, makes clear that "other molecules" include "DNA, mRNA, sugars, proteins, peptides, membrane impermeable drugs" etc. Clearly, the teachings encompass the internalization of molecules other than just molecules intended to induce the death of the cells. Also consider that it would be nonsensical to describe a method of maintaining cell viability if the only intended end result was the death of the cell. Second, Applicant is again reminded that the instant claims are not drawn to a method of treating cancer, But rather, a method of "presenting an antigenic peptide on the surface of a viable cancer cell" (Claim 2).

6. No claim is allowed.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated

from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ram Shukla, can be reached on (571) 272-0878.

9. **Please Note:** Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

/G.R. Ewoldt/
G.R. Ewoldt, Ph.D.
Primary Examiner
Technology Center 1600